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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/762,183	01/20/2004	Guy M. Miller	104732000601	4937

38706 7590 03/15/2006

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EXAMINER	
LEWIS, AMY A	

ART UNIT	PAPER NUMBER
1614	

DATE MAILED: 03/15/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/762,183	MILLER ET AL.	
	Examiner	Art Unit	
	Amy A. Lewis	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 January 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-57* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-57* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *20 January 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *12/2/2004*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of the Case

Claims 1-57, as filed on 20 January 2004, are currently examined.

Priority to provisional application 60/256269, filed 15 December 2000, and provisional application 60/296580, filed 6 June 2001, is acknowledged.

The petition to add the inventor Parto Khansari, filed 26 March 2004, has been accepted.

Objection to the Specification

The status of the parent case(s) should be updated; information regarding the status as a continuation of Application Serial No. 10/020450 should be included in the "Cross-Reference to Related Applications" section of the specification.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

1) Claims 1-57 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-40 of copending Application Serial No. 10/017717 (US Patent Application Pub. No. US 2002/0132845 A1). Although the conflicting claims are not identical, they are not patentably distinct from each other because they both teach a method for treating and/or ameliorating the symptoms of a cerebral ischemic condition in a mammal by administering a non-alpha tocopherol composition.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

2) Claims 1-57 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-40 of copending Application Serial No. 10/020450 (US Patent Application Pub. No. US 2002/0143049). Although the conflicting claims are not identical, they are not patentably distinct from each other because they both teach a method for treating and/or ameliorating the symptoms of a cerebral ischemic condition in a mammal by administering a non-alpha tocopherol composition.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

3) Claims 1-57 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wechter W (US Patent Application Pub. No. US 2004/0029954 A1).

Wechter broadly claims methods of treating or preventing any ischemic condition comprising administering a composition comprising tocopherols, at least 50% of which being γ-tocopherol. The reference also teaches administration of γ-tocopherol derivatives, including the γ-tocopherol metabolite LLU-α (also known as gamma-CEHC; see Wechter WJ "A new endogenous natriuretic factor: LLU-α," June 1996 *PNAS* 93: 6002-6007, cited for definition purposes only). Claimed ischemic conditions include those associated with the brain, the nervous system and the eye (see: paragraphs [0026]). The reference also teaches treatment of thromboembolic disease, cardiovascular disease, neurological lesions, and reperfusion injury (see paragraphs [0002], [0011], and [0023-0026]).

The claims differ in that the present claims recite "a non-alpha tocopherol enriched tocopherol composition" and "for treating and/or ameliorating a symptom of neuronal damage associated with a cerebral ischemic condition". However, one skilled in the art would have

considered the recited compositions, "a non-alpha tocopherol enriched tocopherol composition" to comprise other tocopherols. The open language of the present claims allows for the addition of any number of other active ingredients in the composition. Further, it would have been reasonable to expect an improvement in an ischemic condition of the brain, i.e., an improvement in blood supply to the brain (i.e. reperfusion), would result in a reduction of neuronal damage associated with ischemia. The determination of optimal concentrations and optimal dosage forms are parameters well within the purview of those skilled in the art through no more than routine experimentation.

Claim Rejections - 35 USC § 112, 1st paragraph
Scope of enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

1) Claims 1-20 and 25 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treatment and or amelioration of ***some*** symptoms of a cerebral ischemic condition due to occlusion of the MCAO artery, with the gamma tocopherol metabolite CEHC, the specification does not reasonably provide enablement for treating and/or ameliorating ***all*** symptoms of a cerebral ischemic condition with all non-alpha tocopherol compounds and/or metabolites. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

Attention is directed to *In re Wands*, 8 USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing *Ex parte Forman*, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors:

1) Nature of the invention.
2) State of the prior art.
3) Level of predictability in the art.
4) Relative skill of those in the art.
5) Amount of direction or guidance provided by the inventor.
6) Presence or absence of working examples.
7) Breadth of the claims.
8) Quantity of experimentation necessary to make or use the invention based on the content of the disclosure.

The instant specification fails to provide guidance that would allow the skilled artisan to practice the instant invention without resorting to undue experimentation, as discussed in the subsections set forth hereinbelow.

1) The nature of the invention.

The claimed invention relates to a method of treating and or ameliorating the symptoms of a cerebral ischemic condition.

2) State of the prior art & 3) Level of predictability in the art.

While the state of the art is relatively high with regard to the treatment and/or amelioration of various symptoms of cerebral ischemic conditions, the state of the art with regard to treating all symptoms is underdeveloped (see: Cecil, Textbook of Medicine, 21st Edition (2000), Goldman & Bennett (Editors), W.B. Saunders Company (Publisher), Chapter 470 & 471, pages 2099-2115).

In addition, the level of predictability regarding outcome of treatment and/or

amelioration of a cerebral ischemic condition is unpredictable, see Cecil p. 2106-2108, and 2115 regarding treatment and prognosis.

The lack of significant guidance from the present specification or prior art with regard to the treatment and/or amelioration of all symptoms of cerebral ischemic conditions with the claimed active ingredients makes practicing the claimed invention of prevention unpredictable.

4) Relative skill of those in the art.

The relative skill of those in the art is high, generally that of a PHD/MD with several years of practical experience.

5) Amount of direction or guidance provided by the inventor & 6) Presence or absence of working examples.

The specification teaches the specific treatment of Sprague Dawley rats who have undergone an ischemic stroke due to occlusion of the middle cerebral artery with the gamma-tocopherol metabolite CEHC. Symptoms evaluated include motor symptoms (such as forelimb flexion, resistance to lateral pushing, grip strength, and ability to perform on a treadmill), increased body temperature, as well as size of infarct volume However, it does not teach prevention or the use of any of the other compounds listed in claim 1. See: Example 2, pages 61-74, Figures 1, 2 and 4.

7) Breadth of claims.

The claims are very broad and inclusive of treatment and/or amelioration of any and all symptoms of cerebral ischemic conditions in general. The breadth of the claims exacerbates the complex nature of the subject matter to which the present claims are

directed. The claims are extremely broad due to the various pathologies and symptoms which can result from cerebral ischemia. In addition, as written, the claims include treatment and/or amelioration of death due to cerebral ischemia; a symptom for which the specification is not enabled for treating or ameliorating.

8) Quantity of experimentation needed to make or use the invention based on the content of the disclosure.

The specification does not enable any person skilled in the art to which it pertains (i.e. treatment and/or amelioration of any and all symptoms of cerebral ischemic conditions) to make or use the invention commensurate in scope with the claims. The lack of adequate guidance from the specification or prior art with regard to the actual treatment and/or amelioration of any and all symptoms of cerebral ischemic conditions fails to rebut the presumption of unpredictability existent in this art. Applicants fail to provide the guidance and information required to ascertain a treatment which will treat such episodes without resorting to undue experimentation. Applicant's limited disclosure with respect to the gamma-tocopherol metabolite CEHC (see specification at Example 2, pages 61-74, Figures 1, 2 and 4) is noted but does not demonstrate treatment and/or amelioration of any and all symptoms of cerebral ischemic conditions.

Absent a reasonable *a priori* expectation of success for using non-alpha tocopherol compounds, and any metabolites thereof, to treat and/or ameliorate of any and all symptoms of cerebral ischemic conditions, one skilled in the art would have to extensively test many various compounds under various conditions and degrees of severity of cerebral ischemic conditions.

Since each prospective embodiment, and indeed future embodiments as the art progresses, would have to be empirically tested, and those which initially failed tested further, an undue amount of experimentation would be required to practice the invention as its is claimed in its current scope, because the specification provides inadequate guidance to do otherwise.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 15-50 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claims recite various perventages of tocopherol in the composition, however it is not clear as to what the percentages represent: i.e. percent by weight.

Pertinent Art:

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

- Saldeen T, et al. "Differential Effects of α- and γ-Tocopherol on low-density lipoprotein oxidation...," 1999 *J American College of Cardiology* 34(4): 1208-1215. The reference discusses the superiority of γ-tocopherol over α-tocopherol in decreasing thrombus formation.

Conclusion

Claims 1-57 are rejected. No claims are allowed.

Contact Information:

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Amy A. Lewis whose telephone number is (571) 272-2765. The examiner can normally be reached on Monday-Friday, 9:00-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached on (571) 272-0951. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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